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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/640,935	08/17/2000	Michael S. Kinch	3220-66874	3254

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EXAMINER	
YU, MISOOK	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 03/09/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/640,935	KINCH ET AL.	
	Examiner	Art Unit	
	MISOOK YU, Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 November 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *58-102* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *58-102* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *11/24/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 11/24/2003 has been entered.

Claims 58-102 are pending and examined on merits.

This Office action contains new grounds of rejection.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

Information Disclosure Statement

The requested copy of the previous 1449 is attached with this Office action. 1449 from the IDS filed on 11/24/2003 are also attached with this Office action.

Specification

The objection to the specification is withdrawn based on applicant's response filed on 11/24/2003.

Claim Rejections - 35 USC § 112

Claims 58-71, 101, and 102 remain rejected for reason of record under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the

inventor(s), at the time the application was filed, had possession of the claimed invention. The **rejection of claims 72-100**, drawn to method using a genus of anti-EphA2 antibodies with the recited function **is withdrawn** because the art knows how to make antibody directed to a known protein sequence and the antibody with the function could be screened.

This written description is made because claims 58-71, 101, and 102 are drawn to method using a genus of product recited as "a compound that increases the phosphotyrosine content of EphA2".

Applicant argues that "a compound" that increases the phosphotyrosine content of EphA2" could be screened easily based on teachings of the instant specification and the compounds to be screened could be obtained from a commercial vendor as in the case of Koolpe et al. The argument is fully considered but found not persuasive.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claim is a function of "a compound". The specification discloses that the ligand (EphrinA1) and an anti-EphA2 antibody have the recited function. Dr. Kinch's Declaration filed on 11/24/2003 also discloses two more monoclonal antibodies to EphA2 with the recited function. However,

this rejection is still maintained because anti-EphA2 antibodies and the ligand do not share common core structure so as to be representative of a genus called "compound". The court recently decided in UNIVERSITY OF ROCHESTER, v. G.D. SEARLE & CO., INC., MONSANTO COMPANY, PHARMACIA CORPORATION, and PFIZER INC., (CAFC, decided February 13, 2004) that teaching how to screen a compound does not satisfy written description. There is not even identification of any common structure that has the recited function. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of compound, given that the specification has an anti-EphA2 antibody and EphrinA1. Therefore, only the ligand (EphrinA1) and anti-EphA2 antibodies, but not the full breadth of the claim meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 U.S.C. §112 is separable from its enablement provision (see page 1115).

A definition by function alone "does not suffice, to sufficiently describe a coding sequence "because it is only an indication of what the gene does, rather than what it is." *Eli Lily*, 119 F.3 at 1568, 43 USPQ2d at 1406. Also note UNIVERSITY OF ROCHESTER, v. G.D. SEARLE & CO., INC., MONSANTO COMPANY, PHARMACIA CORPORATION, and PFIZER INC., (CAFC, decided February 13, 2004).

Claims 58-102 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. This rejection has several aspects.

Applicant argues that screening a wide variety of additional compounds capable of increasing the phosphotyrosine content of EphA2 in cancer cells could be accomplished based on the teachings of the instant specification and others in the art, Koope et al, following the procedures disclosed in the specification have been able to screen a compound (that has the recited function) from a commercially available library.

These arguments and Dr. Kinch's data have been fully considered but found unpersuasive for following reasons.

First, this enablement rejection is made because claims 58-102 are interpreted as drawn to method of reducing tumor metastasis (see claims rejection under 112, second paragraph, for why the claims are interpreted as drawn to method of reducing tumor metastasis). Neither the specification nor the data filed during the prosecution of

the instant application has shown that the claimed method is effective for reducing metastasis. The in vivo data presented in Dr. Kinch's declaration filed on 11/24/2003 are enable for treating primary tumor by reducing tumor volume but it does not appear to reduce metastasis of tumor. Hill (The Basic Science of Oncology, Tannock et al., Eds, McGraw Hill, NY, 1992, pp 178-195) teaches at page 178 under the heading INTRODUCTION that clinicians have been relatively successful in treating localized tumors, but less successful in getting rid of metastasis of tumors. Hill teaches the in vivo metastasis assay at Fig. 11.8 at page 185. Applicant is invited to present data showing administering the claimed products (anti-EphA2 antibody or EphrinA2) reduces metastasis in an art-accepted vivo metastasis assay such, the assay shown in Fig. 11.8 of Hill (or other equivalent assay) in order to obviate this part of enablement rejection. Alternatively, amending the preambles to "method of treating" and/or amending the effect of active steps to "reduce tumor volume" would also obviate this part of enablement rejection.

Second, claims 58-71, and 101 are drawn to method of treating a patient having a metastatic tumor with "a compound that increases the phophotyrosine content of EphA2". It is the Office's position that the ability to make and screen is not standard for enabling disclosure. The standard is to make and use. As stated in the previous Office action mailed on 08/14/2002 (note the paragraph bridging pages 8-9), most cancer treating drugs were discovered by serendipity. Trial and error approach requires undue experimentation. The two species i.e. EphrinA1-Fc and the anti- EphA2 antibodies do not appear to have in common structures such that one would predictably be able to

make compounds with the recited function. Limiting the scope to a compound with common structure to EphrinA1 and/or anti- EphA2 antibody with the recited function would obviate this rejection.

The rejection of claims under 35 U.S.C. 112, first paragraph, scope of enablement is **withdrawn** because it is redundant given the enablement rejection above.

The Following Are New Grounds of Rejection

Claims 62-65, 69-71, 79-88, and 95-102 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 62-65, and 79-88, 101, and 102 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: a step that accomplishes the purpose stated in the preamble of the claims. The preamble of the claims says that the invention is drawn to method of treating a patient having a metastatic tumor.

Claims 62, 69, 79, and 95 are confusing because it is not clear whether the active steps will result in reduction in formation of to form metastases (i.e. to form a new foci of growth at noncontiguous sites) or kills already metastasized tumor cells. All dependent claims are rejected because they depend on the rejected base claims.

For this Office action, the Office interprets the active steps is to reduce formation a new foci of tumor growth at noncontiguous sites. However, this treatment does not relieve applicant the burden of responding to this rejection.

Claim Rejections - 35 USC § 112

Claims 58-102 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is new matter rejection because the specification as originally filed does not have a support the limitation for "a compound that increases the phosphorylation content of EphAA2". Applicant argues at page 10 of the amendment filed on 12/19/2003 that the support is at page 3 lines 1-6. However, the specification at page 3 lines 1-6 describes EphrinA1-Fc can be used to increase the phophorylation content of EphA2 but does not have support for "a compound that increases the phosphorylation content of EphAA2". The specification at page 3 lines 18 describes "compound that specifically interacts with an extracellular epitope of EphA2" but does not have support for "a compound that increases the phosphorylation content of EphAA2".

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MISOOK YU, Ph.D. whose telephone number is 571-

272-0839. The examiner can normally be reached on 8 A.M. to 5:30 P.M., every other Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne C Eyler can be reached on 571-272-0871. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

MISOOK YU, Ph.D.
Examiner
Art Unit 1642

LARRY R. HELMS, PH.D
PRIMARY EXAMINER